

AMENDMENTS TO THE SPECIFICATION

By the foregoing amendment, the applicants have complied with the Sequence Listing rules by replacing the Sequence Listing of record with a substitute Sequence Listing, introducing SEQ ID numbers (SEQ ID NO: 40 and SEQ ID NO: 41) corresponding to new sequences (see enclosed computer readable copy, hard copy of the Sequence Listing, and Sequence Listing statement). The changes embodied in the substitute Sequence Listing pertain only to compliance with formatting rules and find support throughout the text of the specification.

The description in the <223> field for amino acid position 500 for SEQ ID NO: 1 ("Xaa is Asn or Ser Thr or Lys") has been amended to --Xaa is Asn or Ser ~~or~~ Thr or Lys-, therefore correcting a typographical error.

Also, the "Raw Sequence Listing Error Report" indicated that sequences in the sequence listing contain Xaa's representing more than one residue, which does not comply with patent sequence rules. Per sequence rules, Xaa can only represent a single residue.

Particularly, the <223> field for amino acid position 107 of SEQ ID NO: 1 and SEQ ID NO: 2 identified Xaa as Asp-Arg or missing. In order to comply with the sequence rules, the <223> field for amino acid position 107 of SEQ ID NO: 1 and SEQ ID NO: 2 has been amended to recite "Xaa is missing," thereby correcting the variable length sequences (e.g. "Xaa is Asp-Arg or missing") and properly identifying Xaa as missing at position 107.

In addition, two new sequences have been added (similar to SEQ ID NOs: 1 and 2 but which now include a di-peptide at position 107). Specifically, amino acids Asp and Arg (Asp-Arg) are continuous amino acids within the sequence of SEQ ID NO: 1 and

SEQ ID NO:2 beginning at amino acid position 107, therefore the sequence listing has been revised to introduce new sequences of SEQ ID NO: 40 and SEQ ID NO: 41, which correspond to SEQ ID NO: 1 and SEQ ID NO: 2, respectively to define amino acid position 107 as Asp-Arg (thus creating new sequences wherein there is one additional amino acid).

AMENDMENT TO THE CLAIMS

By the foregoing amendment to the claims, the applicants have simply rewritten the claims to correct minor informalities to add sequence identification numbers (*i.e.*, with respect to SEQ ID NOS: 40 and 41). Therefore, no new matter has been added.

III. CONCLUSION

In view of the foregoing, the applicants respectfully request that substantive examination be undertaken.

Respectfully submitted,

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APPENDIX A

MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

The paragraph at page 5, lines 20-21 has been replaced with the following rewritten paragraph:

Hence the present invention makes available a process for the production of a mistletoe lectin polypeptide or a fragment thereof in the heterologous system having the following sequence (SEQ ID NO: 1 and 40):

The paragraph at page 7, at lines 5-7 has been replaced with the following rewritten paragraph:

Analogously to this process, two further production processes for the mistletoe lectin A-chain (MLA) (SEQ ID NO: 2 and 41) and mistletoe lectin B-chain (MLB) (SEQ ID NO: 3) are made available, which contain the following sequences or a fragment thereof:

The paragraph at page 8, line 15-16 has been replaced with the following rewritten paragraph:

Furthermore, a mistletoe lectin polypeptide or a fragment thereof, which includes the sequence variability of the various MLA and MLB chains, having the following sequence is provided (SEQ ID NO: 1 and SEQ ID NO: 40):

The paragraph at page 10, at lines 3-5 has been replaced with the following rewritten paragraph:

Apart from this, mistletoe lectin polypeptides of the mistletoe lectin A-chain (SEQ I D NO: 2 and 41) and mistletoe lectin B-chain (SEQ ID NO: 3) or fragments of these sequences are provided, which include the following sequences:

The paragraph at page 20, lines 27-29 has been replaced with the following rewritten paragraph:

Furthermore, the present invention also includes a process for the production of a mistletoe lectin polypeptide in mistletoe cells and/or transgenic mistletoe plants having the following sequence (SEQ ID NO: 1 and 40):

The paragraph at page 22, at lines 20-22 has been replaced with the following rewritten paragraph:

On the basis of the process described above, two further production processes for the mistletoe lectin A-chain (SEQ ID NO: 2 and 41) and mistletoe lectin B-chain (SEQ ID NO: 3) or a fragment thereof are provided, which contain the following sequences or a fragment thereof:

IN THE CLAIMS

46. (Amended) A process for the production of a mistletoe lectin polypeptide in a heterologous system having a polypeptide sequence of SEQ ID NO: 1 and SEQ ID NO: 40 or a fragment thereof, comprising the step of expressing by means of a eukaryotic or prokaryotic vector, in which a nucleic acid coding for the mistletoe lectin polypeptide according to the usual genetic code or a fragment thereof is cloned in a suitable heterologous eukaryotic or prokaryotic host, wherein Xaa at position 533 of SEQ ID NO: 1 and Xaa at position 534 of SEQ ID NO: 40 is phenylalanine.

47. (Amended) The process according to claim 46, wherein the mistletoe lectin polypeptide corresponds to a mistletoe lectin A-chain (MLA) or a fragment thereof, and comprising the polypeptide sequence of SEQ ID NO: 2 and SEQ ID NO: 41, or a fragment thereof.

48. (Amended) The process according to claim 46, wherein the mistletoe lectin polypeptide corresponds to a mistletoe lectin B-chain (MLB) or a fragment thereof, comprising the polypeptide sequence of SEQ ID NO: 3, or a fragment thereof, wherein Xaa at position 533 of SEQ ID NO: 1 and Xaa at position 534 of SEQ ID NO: 40 is phenylalanine.

49. (Amended) A mistletoe lectin polypeptide comprising the sequence of SEQ ID NO: 1 and SEQ ID NO: 40, or a fragment thereof, wherein Xaa at position 533 of SEQ ID NO: 1 and Xaa at position 534 of SEQ ID NO: 40 is phenylalanine.

50. (Amended) The mistletoe lectin polypeptide of claim 49, comprising the sequence of SEQ ID NO: 2 and SEQ ID NO: 41 or a fragment thereof, wherein the mistletoe lectin polypeptide corresponds to the MLA chain or a fragment thereof.

51. (Amended) The mistletoe lectin polypeptide of claim 49, comprising the sequence of SEQ ID NO: 3 or a fragment thereof, wherein the mistletoe lectin polypeptide corresponds to the MLB chain or a fragment thereof, wherein Xaa at position 533 of SEQ ID NO: 1 and Xaa at position 534 of SEQ ID NO: 40 is phenylalanine.

85. (Amended) A process for the production of a mistletoe lectin polypeptide in mistletoe cells and/or a transgenic mistletoe plant having the sequence of SEQ ID NO: 1 and SEQ ID NO: 40 or a fragment thereof, comprising the step of expressing by means of a eukaryotic vector, which contains a nucleic acid coding for the mistletoe lectin polypeptide or a fragment thereof having the nucleic acid sequence originally found in mistletoe cell DNA, in a mistletoe cell and/or a transgenic mistletoe plant, wherein the transcription product of this nucleic acid molecule is modified in mistletoe cells and/or transgenic mistletoe plants by post-transcriptional and/or post-translational mechanisms, wherein Xaa at position 533 of SEQ ID NO: 1 and Xaa at position 534 of SEQ ID NO: 40 is phenylalanine.

86. (Amended) The process of claim 85, wherein the mistletoe lectin polypeptide corresponds to the mistletoe lectin A-chain or a fragment thereof and includes the sequence of SEQ ID NO: 2 and SEQ ID NO: 41, or a fragment thereof.

87. (Amended) The process of claim 40, wherein the mistletoe lectin polypeptide corresponds to the mistletoe lectin B-chain or a fragment thereof and includes the sequence of SEQ ID NO: 3, or a fragment thereof wherein Xaa at position 533 of SEQ ID NO: 1 and Xaa at position 534 of SEQ ID NO: 40 is phenylalanine.

APPENDIX B

PENDING CLAIMS AFTER ENTRY OF AMENDMENT HEREIN

46. (Amended) A process for the production of a mistletoe lectin polypeptide in a heterologous system having a polypeptide sequence of SEQ ID NO: 1 and SEQ ID NO: 40 or a fragment thereof, comprising the step of expressing by means of a eukaryotic or prokaryotic vector, in which a nucleic acid coding for the mistletoe lectin polypeptide according to the usual genetic code or a fragment thereof is cloned in a suitable heterologous eukaryotic or prokaryotic host, wherein Xaa at position 533 of SEQ ID NO: 1 and Xaa at position 534 of SEQ ID NO: 40 is phenylalanine.

47. (Amended) The process according to claim 46, wherein the mistletoe lectin polypeptide corresponds to a mistletoe lectin A-chain (MLA) or a fragment thereof, and comprising the polypeptide sequence of SEQ ID NO: 2 and SEQ ID NO: 41, or a fragment thereof.

~~48. (Amended) The process according to claim 46, wherein the mistletoe lectin polypeptide corresponds to a mistletoe lectin B-chain (MLB) or a fragment thereof, comprising the polypeptide sequence of SEQ ID NO: 3, or a fragment thereof, wherein Xaa at position 533 of SEQ ID NO: 1 and Xaa at position 534 of SEQ ID NO: 40 is phenylalanine.~~

49. (Amended) A mistletoe lectin polypeptide comprising the sequence of SEQ ID NO: 1 and SEQ ID NO: 40, or a fragment thereof, wherein Xaa at position 533 of SEQ ID NO: 1 and Xaa at position 534 of SEQ ID NO: 40 is phenylalanine.

50. (Amended) The mistletoe lectin polypeptide of claim 49, comprising the sequence of SEQ ID NO: 2 and SEQ ID NO: 41 or a fragment thereof, wherein the mistletoe lectin polypeptide corresponds to the MLA chain or a fragment thereof.

51. (Amended) The mistletoe lectin polypeptide of claim 49, comprising the sequence of SEQ ID NO: 3 or a fragment thereof, wherein the mistletoe lectin polypeptide corresponds to the MLB chain or a fragment thereof, wherein Xaa at position 533 of SEQ ID NO: 1 and Xaa at position 534 of SEQ ID NO: 40 is phenylalanine.

52. The mistletoe lectin polypeptide of claim 49, comprising the sequence of SEQ ID NO: 4.

53. The mistletoe lectin polypeptide of claim 50, comprising the sequence of SEQ ID NO: 38.

54. The mistletoe lectin polypeptide of claim 51, said polypeptide selected from the group consisting of:

- I) a polypeptide comprising the sequence of SEQ ID NO: 6;
- II) a polypeptide comprising the sequence of SEQ ID NO: 7;
- III) a polypeptide comprising the sequence of SEQ ID NO: 8;
- IV) a polypeptide comprising the sequence of SEQ ID NO: 9;
- V) a polypeptide comprising the sequence of SEQ ID NO: 10; and
- VI) a polypeptide comprising the sequence of SEQ ID NO: 11.

55. The process for the preparation of a nucleic acid molecule which codes for a mistletoe lectin polypeptide of claim 49 in a heterologous host, comprising the steps of:

- a) preparing mistletoe cell RNA or chromosomal mistletoe cell DNA;
- b) amplifying mistletoe cell RNA or chromosomal mistletoe lectin DNA by PCR using oligonucleotides which are derived from the mistletoe lectin polypeptide of SEQ ID NO: 4;
- c) if necessary, identifying of sequences which lie 5' and 3' from the amplified nucleic acid and amplification thereof;
- d) isolating of the nucleic acid molecules amplified in step b) and/or c);

e) if necessary, ligating several of the nucleic acid molecules amplified in step b) and/or c), such that a nucleic acid molecule with a complete open reading frame is obtained; and

f) targeted mutation of the nucleic acid molecule obtained in order to match the nucleic acid molecule to the usual genetic code of the heterologous host for one of the mistletoe lectin polypeptide isoforms identified in mistletoe cells.

56. The nucleic acid molecule, coding for a polypeptide of claim 49 and comprising the sequence of SEQ ID NO: 12 or a fragment thereof.

57. The nucleic acid molecule which codes for a polypeptide of claim 50 in a heterologous host, comprising the sequence of SEQ ID NO: 13 or a fragment thereof.

58. The nucleic acid which codes for a polypeptide of claim 51 in a heterologous host, comprising the sequence of SEQ ID NO: 14 or a fragment thereof.

59. The nucleic acid molecule of claim 56, comprising the sequence of SEQ ID NO: 15.

60. The nucleic acid molecule of claim 57, said nucleic acid molecule selected from the group consisting of:

I) a nucleic acid comprising the sequence of SEQ ID NO: 16, or a fragment thereof; and

II) a nucleic acid comprising the sequence of SEQ ID NO: 17, or a fragment thereof.

61. The nucleic acid molecule of claim 58, said nucleic acid molecule selected from the group consisting of:

I) a nucleic acid comprising the sequence of SEQ ID NO: 21, or a fragment thereof;

- II) a nucleic acid comprising the sequence of SEQ ID NO: 22, or a fragment thereof;
- III) a nucleic acid comprising the sequence of SEQ ID NO: 23, or a fragment thereof;
- IV) a nucleic acid comprising the sequence of SEQ ID NO: 24, or a fragment thereof;
- V) a nucleic acid comprising the sequence of SEQ ID NO: 25, or a fragment thereof; and
- VI) a nucleic acid comprising the sequence of SEQ ID NO: 26, or a fragment thereof.

62. The nucleic acid molecule coding for a mistletoe lectin polypeptide of claim 4 or a fragment thereof, wherein the codon usage is adapted to the requirements of a heterologous host.

63. The nucleic acid molecule of claim 62 comprising the sequence of SEQ ID NO: 18, wherein the codon usage is adapted to the preferred codon usage of the genus *Brassica*.

64. The nucleic acid molecule of claim 62, said nucleic acid molecule selected from the group consisting of:

- I) a nucleic acid comprising the sequence of SEQ ID NO: 19; and
- II) a nucleic acid comprising the sequence of SEQ ID NO: 20.

65. The nucleic acid molecule of claim 62, said nucleic acid molecule selected from the group consisting of:

- I) a nucleic acid comprising the sequence of SEQ ID NO: 27;
- II) a nucleic acid comprising the sequence of SEQ ID NO: 28;
- III) a nucleic acid comprising the sequence of SEQ ID NO: 29;

IV) a nucleic acid comprising the sequence of SEQ ID NO: 30;

V) a nucleic acid comprising the sequence of SEQ ID NO: 31; and

VI) a nucleic acid comprising the sequence of SEQ ID NO: 32.

66. A vector comprising a nucleic acid molecule of claim 56 or a fragment thereof and a promoter functionally linked thereto.

67. The vector of claim 66, wherein the promoter is a specific promoter for an intended host cell.

68. The vector of claim 66 or claim 67, wherein the vector is an RNA vector.

69. A host cell for carrying out the process of claim 1, which can be a bacterial cell, a plant cell with the exception of mistletoe cell, an insect larva an insect cell, a vertebrate cell, preferably a mammalian cell, a yeast cell, a fungal cell a transgenic vertebrate and/or a transgenic plant with the exception of a mistletoe plant and contains a nucleic acid molecule of claim 56 or a vector of claim 66.

70. The host cell according to claims 69, wherein the bacterial cell is *Escherichia coli* and/or the plant cell is a rape cell and/or the insect larva cell is *Trichopulsia ni* and/or the insect cell is *Spodoptera frugiperda* cell and/or the vertebrate is a zebra fish.

71. A pharmaceutical composition, containing a nucleic acid molecule of claim 56 or vector of claim 66.

72. The pharmaceutical composition of claim 71, further containing liposomes.

73. The pharmaceutical composition of claim 72, wherein the liposomes bear cell recognition molecules on their surface, and wherein the cell recognition molecule selectively binds to target cells.

74. The pharmaceutical composition of claim 71, further containing MLB polypeptide of claim 51.

75. The pharmaceutical composition of claim 74, wherein the MLB polypeptide, the nucleic acid molecule, or the vector is coupled to a cell recognition molecule, wherein the cell recognition molecule selectively binds to target cells.

76. The pharmaceutical composition of claim 71, wherein the nucleic acid or the vector is associated with a virus particle.

77. The pharmaceutical composition of claim 76, wherein the virus particle bears a cell recognition molecule on its surface, wherein the cell recognition molecule selectively binds to target cells.

78. The pharmaceutical composition which contains the polypeptide of claim 49 and/or a fragment thereof.

79. The pharmaceutical composition of claim 78, further containing a suitable cell recognition molecule, wherein the cell recognition molecule selectively binds to target cells.

80. The pharmaceutical composition of claim 79, wherein the cell recognition molecule is selected from the group comprising antibody molecules or antibody fragments, cell receptor ligands, peptide hormones or fragments thereof.

81. Use of a mistletoe lectin polypeptide of claim 49 and/or a fragment thereof for the production of a medicament for the treatment of uncontrolled cell growth.

82. Use of a mistletoe lectin polypeptide of claim 49 and/or a fragment thereof without cytotoxic activity for the production of a medicament which intensifies the immune reaction.

83. Use of claim 82, wherein the medicament includes a further antigen.

84. Use of claim 83, wherein the further antigen is a tumor-induced antigen, a bacterial or viral antigen.

85. (Amended) A process for the production of a mistletoe lectin polypeptide in mistletoe cells and/or a transgenic mistletoe plant having the sequence of SEQ ID NO: 1 and SEQ ID NO: 40 or a fragment thereof, comprising the step of expressing by means of a eukaryotic vector, which contains a nucleic acid coding for the mistletoe lectin polypeptide or a fragment thereof having the nucleic acid sequence originally found in mistletoe cell DNA, in a mistletoe cell and/or a transgenic mistletoe plant, wherein the transcription product of this nucleic acid molecule is modified in mistletoe cells and/or transgenic mistletoe plants by post-transcriptional and/or post-translational mechanisms, wherein Xaa at position 533 of SEQ ID NO: 1 and Xaa at position 534 of SEQ ID NO: 40 is phenylalanine.

86. (Amended) The process of claim 85, wherein the mistletoe lectin polypeptide corresponds to the mistletoe lectin A-chain or a fragment thereof and includes the sequence of SEQ ID NO: 2 and SEQ ID NO: 41, or a fragment thereof.

87. (Amended) The process of claim 40, wherein the mistletoe lectin polypeptide corresponds to the mistletoe lectin B-chain or a fragment thereof and includes the sequence of SEQ ID NO: 3, or a fragment thereof wherein Xaa at position 533 of SEQ ID NO: 1 and Xaa at position 534 of SEQ ID NO: 40 is phenylalanine.

88. A process for the preparation of a nucleic acid molecule, which codes for a mistletoe lectin polypeptide of claim 49 in a mistletoe cell and/or a transgenic mistletoe plant, comprising the steps of:

- a) preparing of mistletoe cell RNA or chromosomal mistletoe cell DNA;
- b) amplifying mistletoe cell RNA or chromosomal mistletoe lectin DNA by PCR using oligonucleotides which are derived from the mistletoe lectin polypeptide of SEQ ID NO: 4;

- c) if necessary, identifying of sequences which lie 5' and 3' from the amplified nucleic acid and amplification thereof;
- d) isolating of the nucleic acid molecules amplified in step b) and/or c);
- e) if necessary, ligating several of the nucleic acid molecules isolated in step b) and/or c), such that a nucleic acid molecule with a complete open reading frame is obtained; and
- f) if necessary, targeted mutation of the nucleic acid molecule obtained in order to match the nucleic acid molecule to the usual genetic code for one of the mistletoe lectin polypeptide isoforms identified in mistletoe cells and/or to optimize expression.

89. The process for production of a polypeptide of claim 46, including as a further step the modification of sugar side-chains by enzymatic and/or chemical addition, removal and/or modification of one or several side-chains.

90. The process of claim 89, wherein the addition, removal and/or modification of the sugar side-chain leads to matching to the natural proteins.